There were no signs of a pancreatic anomaly on radiographs. Laboratory findings were as follows: Hb 5.0 g/dl, WBC 3.3 × 10^9/L, platelets 34 × 10^9/L and HbF 14.1%. The serum amylase level was normal. Bone marrow aspiration showed hypocellular marrow, fewer than 1% blasts, and dysplastic features in erythroid, granulocytic, and megakaryocytic lineages. The bone marrow karyotype was normal. The diagnosis of FA associated with myelodysplastic syndrome (MDS) was made based on clinical characteristics and further supported by chromosome breakage in peripheral lymphocytes following treatment with mitomycin C. In 1994, allogeneic BMT from the patient's HLA-identical male sibling was performed using low-dose CY (5mg/kg/day × 4) followed by 5-GY total body irradiation as the conditioning regimen. The patient received cyclosporin A (3 mg/kg/day), methotrexate (10 mg/m^2 on day 1; 6 mg/m^2 on days 3, 6, and 11) and prednisolone (0.5 mg/kg/day) for GVHD prophylaxis. Although successful engraftment was confirmed by sex chromosome karyotyping on day 13, the patient had grade III GVHD beginning on day 15 after BMT, with skin, liver, and gut manifestations. Her clinical evolution was further complicated on day 19 by severe pancreatitis of unknown origin. The clinical signs of skin and gastrointestinal GVHD improved to some degree, but pancreatitis was refractory to intensive chemotherapy.

The patient died on day 98 post-graft due to severe pancreatitis. Autopsy showed an acute pancreatitis, with acute GVHD compatible infiltration of lymphocytes, and further revealed a congenital hypoplasia of the pancreas with diffuse fibrosis. Thus, the pancreatitis in this patient might have resulted from acute GVHD induced by a anomalous pancreas. Congenital anomaly of the pancreas and the susceptibility of the pancreas to GVHD have not been fully recognized in FA patients. We must now consider the possibility of pancreatitis associated with GVHD in FA patients after allogeneic BMT.

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Central Nervous System Involvement in Multiple Myeloma

To the Editor: Multiple myeloma (MM) commonly presents with neurologic symptoms when it involves the cranium or vertebrae, but rarely invades the central nervous system (CNS) or meninges. Intracranial and intraspinal myeloma without lesions in the adjacent bone are extremely rare [1].

Between 1975 and 1996, 192 patients (108 men, 84 women, median age 56 years) with MM have been observed. Thirty-two patients (16%) had neurologic findings due to various causes. Of these, three patients had a direct involvement of the CNS. First patient, a 42-year-old man was admitted with headache, nausea, vomiting, and seizures. Computed tomography (CT) showed a tumoral mass in the frontal lobe. He had anemia, a high erythrocyte sedimentation rate, and hyperglobulinemia. Serum immonoelectrophoresis confirmed the presence of a monoclonal IgG protein. A bone marrow examination revealed an increase of plasma cells. The mass was removed surgically. The pathologic examination was consistent with plasmacytoma.

The second patient was a 54-year-old woman who had been followed with IgG myeloma. In the third year of the disease, she presented with weakness and wasting in the hands and arms, loss of arm reflexes, and spastic weakness of the lower extremities. A CT scan showed a cervical intraspinal tumoral mass. Peripheral blood smear revealed the presence of plasma cells. She was in poor general condition and died of sepsis within 1 week. On postmortem examination, the mass proved to be an intraspinal plasmacytoma.

The third patient was a 64-year-old man who was admitted to the hospital after he had had a grand mal convulsion. On a CT scan, left parietal lobe tumoral mass was diagnosed. After investigations, IgA myeloma was diagnosed. Pathologic examination of the mass showed sheets of plasma cells.

Nervous system involvement is frequently seen in patients with MM. The most common manifestations are polyneuropathy and myelopathy secondary to spinal cord compression [2]. Polyneuropathy due to autoimmune mechanisms occurs in 5% of patients with MM [3]. Other less common causes of neurologic dysfunction are myelomatous meningitis, amyloidosis, and sensorimotor polyneuropathy due to a remote effect of plasma cells.

Here we present three MM patients with intraparenchymal plasmacytomas without bone or dural attachment. Intracranial involvement with myeloma occurs in one of three forms: single or multiple cranial nerve palsies due to myelomatous involvement of the base of the skull, intraorbital tumors, and intracranial plasmacytoma [4]. The tumor may be the first sign or may develop during the course of the disease. Although it is a less common finding, when a neurologic symptom is discovered in a patient with MM, intraparenchymal CNS plasmacytoma should be considered in the differential diagnosis.

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When Is Selection Bias Not Selection Bias?

To the Editor: Reports from this institution [1] and others [2,3] demonstrated that clonal cytogenetic abnormalities can be used as prognostic factors for adults with newly diagnosed acute myelogenous leukemia (AML). With conventional chemotherapy, those with "good prognosis" karyotypes (t(15;17), t(8;21) and inv16) have a 30–50% long-term disease-free survival,

TABLE I. Interval Hazard Rates for Relapse or Death in First Remission*

Cytogenetic abnormalities	Time from achieving a complete remission (months)			
	0–6	6–12	12–18	18–24
inv16, t(15;17), t(8;21)	0.07 (61)	0.16 (57)	0.16 (47)	0.03 (35)
Diploid	0.19 (53)	0.21 (43)	0.21 (34)	0.13 (23)
+8, −5, −7, abnormal 11q	0.45 (33)	0.39 (18)	0.09 (11)	0.09 (9)
Other	0.26 (19)	0.46 (14)	0.46 (5)	0.33 (3)
All patients	0.21 (177)[a]	0.23 (141)	0.23 (104)	0.10 (75)

*Numbers in parentheses = number of patients entering the 6-month interval.
[a]Eleven patients had insufficient metaphases for cytogenetic categorization.

while those with "poor prognosis" karyotypes have a median survival of 6–10 months.

Once a patient with AML has achieved a first remission, it may require 2–6 months to identify a donor, obtain financial clearance, get the patient to a transplant center, and complete the pretransplant evaluation. This delay may allow for selection of patients who by virtue of having remained in remission are theoretically more likely to have achieved long-term disease control with conventional chemotherapy alone and may not need to undergo transplantation. Such a selection would also bias the transplant outcome over that for conventional chemotherapy. To address this question, we have assessed the relapse rates at 6-month intervals for patients with AML in first remission after conventional chemotherapy.

From January 1, 1990 to July 1, 1994, 230 adults age 17–55 years of age with newly diagnosed AML received induction chemotherapy [4]. Of these, 177 patients achieved a complete remission (CR) and were followed prospectively without transplantation. With a median follow-up of 32 months, 20% relapsed or died in CR within 6 months of remission, 26% in CR at 6 months relapsed or died in CR at 6–12 months after remission, and 29% in CR at 12 months have subsequently relapsed or died more than 12 months after remission. Hazard rates for treatment failure (relapse or death in remission) for patients in various cytogenetic subgroups calculated according to Simes and Zelen [5] are shown in Table I.

Patients with "good prognosis" cytogenetics and those with a normal karyotype had a relatively constant but low risk of treatment failure through the first 24 months after CR. Within the limits of the small numbers, for patients with "poor prognosis" cytogenetics, the risk of relapse or death in CR was not decreased at 6–12 months after CR in comparison to that for less than 6 months after CR. There were too few patients with more than 12 months of follow-up to determine accurately the hazard of late treatment failure, but it appeared to be low. Patients with "other" karyotypic abnormalities had a constant and moderate risk of treatment failure, but the group was too small and heterogeneous to provide reliable conclusions for individual karyotypic abnormalities.

A number of factors have been cited as contributing to a supposedly inflated survival rate after allogeneic marrow transplantation for AML in first remission [6]. Our findings demonstrate that for patients with AML in first remission with "poor prognosis" cytogenetics, continued remission for 2–6 months after conventional chemotherapy does not support the suggestion that they have a reduced rate of relapse. Even if delayed for 6 months, allogeneic transplantation should still be considered an appropriate treatment option for patients with AML in first remission who have "poor prognosis" karyotypes.

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Childbearing Age Patients With Essential Thrombocythemia: Should They Be Placed on Interferon?

To the Editor: Essential thrombocythemia (ET) is a myeloproliferative disorder of increasing frequency in young adults, since automated blood cell counters have been introduced. Optimal prevention and management of thrombotic and hemorrhagic ET complications in patients under 40 years of age is still a controversial issue [1], especially important in young women willing to be protected from the infertility and teratogenicity that may be caused by conventional myelosuppressive therapy [2]. Although normal pregnancies have been reported in several untreated ET patients, there are investigators who report a significantly higher rate of fetal morbidity and mortality due to placental infarctions during pregnancy in ET [2].

The best treatment of ET during pregnancy has not been establilshed yet: aspirin might have a role but carries an increased hemorrhagic risk, platelet-apheresis is of limited efficacy and anagrelide is a drug not released yet for general use. There are recent reports of normal and successful pregnancies in women with hematologic disorders, including ET-treated and controlled with interferon-α (IFN-α) [3–5], suggesting that this drug might be a therapeutic option, although there are no conclusive data about the metabolism and possible side effects of IFN-α during pregnancy.

We report a 31-year-old woman diagnosed of ET for 6 years, initially with a platelet count of $2,000 \times 10^9$/L and abrupt transitory episodes of blurred vision, well controlled with hydroxyurea and aspirin. Because of her desire to become pregnant, hydroxyurea was discontinued. She was started on a therapeutic trial with IFN-α-2a and, after 2 months, a dose of 3 MU/sc every other day was found necessary to maintain the platelet count below 300×10^9/L. Thereafter, IFN was discontinued and the patient was placed on 200 mg qod of aspirin. Six months later, she became pregnant, and aspirin was withheld. After 2 months of pregnancy, the platelet count was $1,550 \times 10^9$/L and, once informed consent was obtained, IFN-α-2a was started at the dose previously tested of 3 MU/qod. During pregnancy the dose of IFN-α necessary to keep the platelet count below 500×10^9/L was 4,5 MU/day sc, until the delivery. Repeated ultrasound scans showed